

CLAIMS

We claim:

1. A composition comprising a synthetic polymer and a drug, the polymer comprising multiple activated groups.
2. The composition of claim 1 wherein the synthetic polymer has a cyclic core.
3. The composition of claim 2 wherein the cyclic core comprises a six-membered carbocyclic group.
4. The composition of claim 2 wherein the cyclic core comprises an inositol residue.
5. The composition of claim 2 wherein the cyclic core comprises a lactitol residue.
6. The composition of claim 2 wherein the cyclic core comprises a sorbitol residue.
7. The composition of claim 1 wherein the synthetic polymer has a branched chain core.
8. The composition of claim 7 wherein the branched chain core is a polyhydric compound residue.
9. The composition of claim 8 wherein the branched chain core is a glycerol residue.

10. The composition of claim 8 wherein the branched chain core is a pentaerythritol residue.

11. The composition of claim 8 wherein the branched chain core is a diglycerol residue.

12. The composition of claim 7 wherein the branched chain core is a poly(carboxylic acid) compound residue.

13. The composition of claim 7 wherein the branched chain core is a polyamine compound residue.

14. The composition of claim 7 wherein the branched chain core comprises polyamino acid.

15. The composition of claim 1 wherein the synthetic polymer comprises poly(alkylene)oxide.

16. The composition of claim 15 wherein the poly(alkylene)oxide comprises ethylene oxide residues.

17. The composition of claim 15 wherein poly(alkylene)oxide comprises propylene oxide residues.

18. The composition of claim 15 wherein the poly(alkylene)oxide has a molecular weight of about 100 to about 100,000.

19. The composition of claim 15 wherein the poly(alkylene)oxide has a molecular weight of about 1,000 to about 20,000.

20. The composition of claim 15 wherein the poly(alkylene) oxide has a molecular weight of about 1,000 to about 15,000.

21. The composition of claim 15 wherein the poly(alkylene) oxide has a molecular weight of about 1,000 to about 10,000.

22. The composition of claim 15 wherein the poly(alkylene) oxide has a molecular weight of about 1,000 to about 5,000.

23. The composition of claim 15 wherein the poly(alkylene) oxide has a molecular weight of about 7,500 to about 20,000.

24. The composition of claim 15 wherein the poly(alkylene) oxide has a molecular weight of about 7,500 to about 15,000.

25. The composition of claim 17 wherein the poly(alkylene) oxide has a molecular weight of about 7,500 to about 20,000.

26. The composition of claim 1 wherein the polymer has 2-12 activated groups.

27. The composition of claim 26 wherein the polymer has 2 activated groups.

28. The composition of claim 26 wherein the polymer has 3 activated groups.

29. The composition of claim 26 wherein the polymer has 4 activated groups.

30. The composition of claim 26 wherein the polymer has 6 activated groups.
31. The composition of claim 26 wherein the polymer has 9 activated groups.
32. The composition of claim 26 wherein the polymer has 12 activated groups.
33. The composition of claim 1 wherein the activated groups are protein-reactive.
34. The composition of claim 33 wherein the activated groups are reactive with hydroxyl groups.
35. The composition of claim 33 wherein the activated groups are reactive with thiol groups.
36. The composition of claim 33 wherein the activated groups are reactive with amino groups.
37. The composition of claim 1 wherein the activated group comprises an electrophilic site.
38. The composition of claim 37 wherein the electrophilic site is a carbonyl group.
39. The composition of claim 1 wherein the activated group comprises a leaving group.

40. The composition of claim 39 wherein the leaving group is an N-oxysuccinimide group.

41. The composition of claim 39 wherein the leaving group is an N-oxymaleimide group.

42. The composition of claim 1 wherein the activated group comprises an electrophilic site adjacent to a leaving group.

43. The composition of claim 42 wherein the electrophilic site is a carbonyl group.

44. The composition of claim 42 wherein the leaving group is selected from N-oxysuccinimide and N-oxymaleimide.

45. The composition of claim 42 wherein the electrophilic group is carbonyl and the leaving group is selected from N-oxysuccinimide and N-oxymaleimide.

46. The composition of claim 1 wherein the synthetic polymer comprises the formula (polymer backbone)-(Q-Y)_n wherein Q is a linking group, Y is an activated functional group, and n is an integer of greater than 1.

47. The composition of claim 46 wherein the polymer backbone comprises poly(alkylene) oxide.

48. The composition of claim 46 wherein Q is selected from the group consisting of -G-(CH₂)_n- wherein G is selected from O, S, NH, -O-CO- and -O-CO-NH-(CH₂)_n; O₂C-CR¹H- wherein R¹ is selected from hydrogen and alkyl; and O-R²-CO-NH wherein R² is selected from CH₂ and CO-NH-CH₂CH₂.

49. The composition of claim 46 wherein n is 2-12.
50. The composition of claim 46 wherein Y comprises an electrophilic site adjacent to a leaving group.
51. The composition of claim 50 wherein the electrophilic site is a carbonyl group.
52. The composition of claim 50 wherein the leaving group comprises (N-CO-CH₂)₂.
53. The composition of claim 46 wherein the synthetic polymer has the formula (polymer backbone)-(Q-Y)_n.
54. The composition of claim 46 wherein a chain extender is located between either (polymer backbone) and Q or between Q and Y.
55. The composition of claim 1 wherein the synthetic polymer comprises the formula (polymer backbone)-(D-Q-Y)_n wherein D is a biodegradable group, Q is a linking group, Y is an activated functional group, and n is an integer of greater than 1.
56. The composition of claim 55 wherein the polymer backbone comprises poly(alkylene) oxide.
57. The composition of claim 55 wherein D comprises a chemical group selected from lactide, glycolide, epsilon-caprolactone and poly(alpha-hydroxy acid).

58. The composition of claim 55 wherein D comprises a chemical group selected from poly(amino acid), poly(anhydride), poly(orthoester).

59. The composition of claim 55 wherein Q is selected from the group consisting of $-G-(CH_2)_n-$ wherein G is selected from O, S, NH, $-O-CO-$ and $-O-CO-NH-(CH_2)_n$; O_2C-CR^1H- wherein R^1 is selected from hydrogen and alkyl; and $O-R^2-CO-NH$ wherein R^2 is selected from CH_2 and $CO-NH-CH_2CH_2$.

60. The composition of claim 55 wherein Y comprises an electrophilic site adjacent to a leaving group.

61. The composition of claim 60 wherein the electrophilic site is a carbonyl group.

62. The composition of claim 60 wherein the leaving group comprises $(N-CO-CH_2)_2$.

63. The composition of claim 60 wherein the synthetic polymer has the formula (polymer backbone)-(D-Q-Y)_n.

64. The composition of claim 55 wherein a chain extender is located between either (polymer backbone) and Q or between Q and Y.

65. The composition of claim 1 comprising first and second polymers comprising multiple activated groups, where the first and second polymers are non-identical.

66. The composition of claim 65 wherein the first and second polymer comprise different activated groups.

67. The composition of claim 65 wherein the first and second polymers have different number average molecular weights.
68. The composition of claim 65 wherein the first and second polymers have a different number of activated groups.
69. The composition of claim 1 wherein the polymer is soluble in water at a concentration of at least 1 grams polymer/99 grams water at 25°C.
70. The composition of claim 69 wherein the polymer is soluble in water at a concentration of at least 2 grams polymer/99 grams water at 25°C.
71. The composition of claim 69 wherein the polymer is soluble in water at a concentration of at least 3 grams polymer/99 grams water at 25°C.
72. The composition of claim 69 wherein the polymer is soluble in water at a concentration of at least 4 grams polymer/99 grams water at 25°C.
73. The composition of claim 69 wherein the polymer is soluble in water at a concentration of at least 5 grams polymer/99 grams water at 25°C.
74. The composition of claim 1 wherein the drug is efficacious in inhibiting one or a combination of cellular activities selected from the group consisting of cell division, cell secretion, cell migration, cell adhesion, inflammatory activator production and/or release, angiogenesis and free radical formation and/or release.
75. The composition of claim 1 wherein the drug is an angiogenesis inhibitor.

76. The composition of claim 1 wherein the drug is a 5-Lipoxygenase inhibitor or antagonist.

77. The composition of claim 1 wherein the drug is a chemokine receptor antagonist.

78. The composition of claim 1 wherein the drug is a cell cycle inhibitor or an analogue or derivative thereof.

79. The composition of claim 78 wherein the cell cycle inhibitor is a microtubule stabilizing agent.

80. The composition of claim 79 wherein the microtubule stabilizing agent is paclitaxel, docetaxel, or Peloruside A.

81. The composition of claim 78 wherein the cell cycle inhibitor is a taxane.

82. The composition of claim 81 wherein the taxane is paclitaxel or an analogue or derivative thereof.

83. The composition of claim 78 wherein the cell cycle inhibitor is an antimetabolite, an alkylating agent, or a vinca alkaloid.

84. The composition of claim 83 wherein the vinca alkaloid is vinblastine, vincristine, vincristine sulfate, vindesine, vinorelbine, or an analogue or derivative thereof.

85. The composition of claim 78 wherein the cell cycle inhibitor is camptothecin or an analogue or derivative thereof.

86. The composition of claim 78 wherein the cell cycle inhibitor is selected from the group consisting of mitoxantrone, etoposide, 5-fluorouracil, doxorubicin, methotrexate, Mitomycin-C, CDK-2 inhibitors, and analogues and derivatives thereof.

87. The composition of claim 1 wherein the drug is a cyclin dependent protein kinase inhibitor or an analogue or derivative thereof.

88. The composition of claim 1 wherein the drug is an EGF (epidermal growth factor) kinase inhibitor or an analogue or derivative thereof.

89. The composition of claim 1 wherein the drug is an elastase inhibitor or an analogue or derivative thereof.

90. The composition of claim 1 wherein the drug is a factor Xa inhibitor or an analogue or derivative thereof.

91. The composition of claim 1 wherein the drug is a farnesyltransferase inhibitor or an analogue or derivative thereof.

92. The composition of claim 1 wherein the drug is a fibrinogen antagonist or an analogue or derivative thereof.

93. The composition of claim 1 wherein the drug is a guanylate cyclase stimulant or an analogue or derivative thereof.

94. The composition of claim 1 wherein the drug is a heat shock protein 90 antagonist or an analogue or derivative thereof.

95. The composition of claim 1 wherein the drug is an HMGCoA reductase inhibitor or an analogue or derivative thereof.

96. The composition of claim 1 wherein the drug is a hydroorotate dehydrogenase inhibitor or an analogue or derivative thereof.

97. The composition of claim 1 wherein the drug is an IKK2 inhibitor or an analogue or derivative thereof.

98. The composition of claim 1 wherein the drug is an IL-1, ICE, or IRAK antagonist or an analogue or derivative thereof.

99. The composition of claim 1 wherein the drug is an IL-4 agonist or an analogue or derivative thereof.

100. The composition of claim 1 wherein the drug is an immunomodulatory agent.

101. The composition of claim 1 wherein the drug is an inosine monophosphate dehydrogenase inhibitor or an analogue or derivative thereof.

102. The composition of claim 1 wherein the drug is a leukotriene inhibitor or an analogue or derivative thereof.

103. The composition of claim 1 wherein the drug is a MCP-1 antagonist or an analogue or derivative thereof.

104. The composition of claim 1 wherein the drug is a MMP inhibitor or an analogue or derivative thereof.

105. The composition of claim 1 wherein the drug is a NF kappa B inhibitor or an analogue or derivative thereof.

106. The composition of claim 1 wherein the drug is a NO antagonist or an analogue or derivative thereof.

107. The composition of claim 1 wherein the drug is a P38 MAP kinase inhibitor or an analogue or derivative thereof.

108. The composition of claim 1 wherein the drug is a phosphodiesterase inhibitor or an analogue or derivative thereof.

109. The composition of claim 1 wherein the drug is a TGF beta Inhibitor or an analogue or derivative thereof.

110. The composition of claim 1 wherein the drug is a thromboxane A2 antagonist or an analogue or derivative thereof.

111. The composition of claim 1 wherein the drug is a TNFa Antagonist, a TACE, or an analogue or derivative thereof.

112. The composition of claim 1 wherein the drug is a tyrosine kinase inhibitor or an analogue or derivative thereof.

113. The composition of claim 1 wherein the drug is a vitronectin inhibitor or an analogue or derivative thereof.

114. The composition of claim 1 wherein the drug is a fibroblast growth factor inhibitor or an analogue or derivative thereof.

115. The composition of claim 1 wherein the drug is a protein kinase inhibitor or an analogue or derivative thereof.

116. The composition of claim 1 wherein the drug is a PDGF receptor kinase inhibitor or an analogue or derivative thereof.

117. The composition of claim 1 wherein the drug is an endothelial growth factor receptor kinase inhibitor or an analogue or derivative thereof.

118. The composition of claim 1 wherein the drug is a retinoic acid receptor antagonist or an analogue or derivative thereof.

119. The composition of claim 1 wherein the drug is a platelet derived growth factor receptor kinase inhibitor or an analogue or derivative thereof.

120. The composition of claim 1 wherein the drug is a fibrinogen antagonist or an analogue or derivative thereof.

121. The composition of claim 1 wherein the drug is an antimycotic agent or an analogue or derivative thereof.

122. The composition of claim 1 wherein the drug is a bisphosphonate or an analogue or derivative thereof.

123. The composition of claim 1 wherein the drug is a phospholipase A1 inhibitor or an analogue or derivative thereof.

124. The composition of claim 1 wherein the drug is a histamine H1/H2/H3 receptor antagonist or an analogue or derivative thereof.

125. The composition of claim 1 wherein the drug is a macrolide antibiotic or an analogue or derivative thereof.

126. The composition of claim 1 wherein the drug is an GPIIb IIIa receptor antagonist or an analogue or derivative thereof.

127. The composition of claim 1 wherein the drug is an endothelin receptor antagonist or an analogue or derivative thereof.

128. The composition of claim 1 wherein the drug is a peroxisome proliferators-activated receptor agonist or an analogue or derivative thereof.

129. The composition of claim 1 wherein the drug is an estrogen receptor agent or an analogue or derivative thereof.

130. The composition of claim 1 wherein the drug is somatostatin or an analogue or derivative thereof.

131. The composition of claim 1 wherein the drug is a JNK Kinase inhibitor or an analogue or derivative thereof.

132. The composition of claim 1 wherein the drug is a melanocortin analogue or derivative thereof.

133. The composition of claim 1 wherein the drug is a raf kinase inhibitor or analogue or derivative thereof.

134. The composition of claim 1 wherein the drug is a lysylhydroxylase inhibitor or an analogue or derivative thereof.

135. The composition of claim 1 wherein the drug is an IKK 1/2 inhibitor or an analogue or derivative thereof.

136. The composition of claim 74 wherein the drug is a cytokine modulator.

137. The composition of claim 74 wherein the drug is a cytokine antagonist.

138. The composition of claim 1 wherein the drug is water-insoluble.

139. The composition of claim 1 in anhydrous form.

140. The composition of claim 1 in sterile form.

141. The composition of claim 1 wherein the polymer contributes about 0.5-40 percent of the weight of the composition.

142. The composition of claim 1 further comprising a solvent.

143. The composition of claim 142 wherein the solvent comprises water.

144. The composition of claim 1 further comprising a buffer.

145. The composition of claim 144 wherein the buffer maintains the pH of the composition within the range of 4-10.

146. The composition of claim 144 wherein the buffer maintains the pH of the composition within the range of 5-9.

147. The composition of claim 144 wherein the buffer maintains the pH of the composition within the range of 6-8.

148. The composition of claim 144 wherein the buffer comprises phosphate.

149. The composition of claim 1 further comprising protein.

150. The composition of claim 149 wherein the protein is collagen.

151. The composition of claim 149 wherein the protein contains primary amino groups.

152. The composition of claim 1 further comprising polysaccharide.

153. The composition of claim 152 wherein the polysaccharide is glysoaminoglycan.

154. A method of affecting biological processes *in vivo* comprising:

- a) selecting an *in vivo* biological tissue comprising functional groups X;
- b) providing a composition comprising a synthetic polymer and a drug, the polymer comprising multiple activated groups Y, where Y is reactive with X;
- c) contacting the tissue of step a) with the composition of step b) under conditions where i) X reacts with Y and ii) biological processes in the vicinity of the tissue are affected by the drug.

155. The method of claim 154 wherein the biological tissue has undergone surgical trauma prior to being contacted with the composition of step b), thereby placing the tissue at risk of adhesion formation.

156. The method of claim 155 wherein the adhesion formation is an undesired by-product of abdominal surgery.

157. The method of claim 155 wherein the adhesion formation is an undesired by-product of cardiac surgery.

158. The method of claim 155 wherein the adhesion formation is an undesired by-product of spinal surgery.

159. The method of claim 155 wherein the adhesion formation is an undesired by-product of nasal surgery.

160. The method of claim 155 wherein the adhesion formation is an undesired by-product of throat surgery.

161. The method of claim 155 wherein the adhesion formation is an undesired by-product of breast implant.

162. The method of claim 155 wherein the biological tissue has undergone surgical trauma prior to being contacted with the composition of step b), the surgery being performed to excise tumor.

163. The method of claim 162 wherein the surgery is breast surgery.

164. The method of claim 162 wherein the surgery is breast tumor lumpectomy.

165. The method of claim 162 wherein the surgery is brain surgery.

166. The method of claim 162 wherein the surgery is hepatic resection surgery.

167. The method of claim 162 wherein the surgery is colon tumor resection surgery.

168. The method of claim 162 wherein the surgery is neurosurgical tumor resection.

169. The method of claim 154 wherein tissue is the interior surface of a physiological lumen.

170. The method of claim 169 wherein the tissue is a blood vessel.

171. The method of claim 169 wherein the tissue is a Fallopian tube.

172. The method of claim 169 wherein the tissue has undergone balloon catheterization.

173. A method comprising:

- a) contacting tissue *in vivo* with a synthetic polymer comprising multiple activated groups, where the activated groups are tissue-reactive;
- b) reacting the synthetic polymer with the tissue so as to covalently adhere the synthetic polymer to the tissue.

174. The method of claim 173 wherein tissue is a blood vessel.

175. The method of claim 173 wherein the tissue is prone to restenosis.

176. The method of claim 173 wherein adhesion of the tissue to secondary tissue is mitigated upon reacting the synthetic polymer with the tissue.

177. The method of claim 173 wherein the tissue does not react with any other synthetic polymer.

178. The method of claim 173 wherein the synthetic polymer is not in admixture with any other polymer that is reactive with the synthetic polymer.

179. The method of claim 173 wherein the synthetic polymer is not in admixture with any other polymer that is reactive with the tissue.

180. The method of claim 173 wherein the synthetic polymer comprises alkylene oxide residues.

181. The method of claim 173 wherein the synthetic polymer is a 4-arm PEG.

182. The method of claim 173 wherein the synthetic polymer comprises a plurality of thiol-reactive groups.

183. The method of claim 173 wherein the synthetic polymer comprises a plurality of hydroxyl-reactive groups.

184. The method of claim 173 wherein the synthetic polymer comprises a plurality of amine-reactive groups.

185. A method comprising:

- a) contacting a non-living surface with a synthetic polymer comprising multiple activated groups, where the activated groups are tissue-reactive;
- b) reacting the synthetic polymer with the surface so as to covalently adhere the synthetic polymer to the surface.

186. The method of claim 185 wherein the surface is a surface of a catheter.

187. The method of claim 185 wherein the surface is a surface of a contact lens.

188. The method of claim 185 wherein adhesion of the surface to living tissue is mitigated upon reacting the synthetic polymer with the surface.

189. The method of claim 185 wherein the surface is not reacted with any other synthetic polymer.

190. The method of claim 185 wherein the synthetic polymer is not in admixture with any other polymer that is reactive with the synthetic polymer.

191. The method of claim 185 wherein the synthetic polymer is not in admixture with any other polymer that is reactive with the surface.

192. The method of claim 185 wherein the synthetic polymer comprises alkylene oxide residues.

193. The method of claim 185 wherein the synthetic polymer is a 4-arm PEG.

194. The method of claim 185 wherein the synthetic polymer comprises a plurality of thiol-reactive groups.

195. The method of claim 185 wherein the synthetic polymer comprises a plurality of hydroxyl-reactive groups.

196. The method of claim 185 wherein the synthetic polymer comprises a plurality of amine-reactive groups.

197. A method for preparing a reactive composition, the method comprising:

- a) providing a synthetic polymer comprising multiple activated groups;
- b) combining the synthetic polymer with a buffer having a pH of less than 6 to form a homogeneous solution; and
- c) raising the pH of the homogeneous solution to a pH of more than about 7.8, thereby rendering the synthetic polymer reactive.

198. The method of claim 197 wherein the synthetic polymer comprises alkylene oxide residues.

199. The method of claim 197 wherein the synthetic polymer comprises thiol-reactive groups.

200. The method of claim 198 wherein the synthetic polymer comprises *N*-oxysuccinimidyl groups.

201. The method of claim 198 wherein the synthetic polymer is combined with a drug.

202. The method of claim 201 wherein the drug is hydrophobic.

203. The method of claim 202 wherein the drug is in association with a secondary carrier, and the secondary carrier is dispersed in aqueous media.

204. A method of adhering a synthetic polymer to *in vivo* tissue, the method comprising:

- a) providing a synthetic polymer comprising multiple activated groups;
- b) combining the synthetic polymer with a buffer having a pH of less than 6 to form a homogeneous solution;
- c) raising the pH of the homogeneous solution to a pH of more than about 7.8, thereby rendering the synthetic polymer reactive; and
- d) contacting the reactive synthetic polymer with *in vivo* tissue.

205. The method of claim 204 wherein the synthetic polymer comprises alkylene oxide residues.

206. The method of claim 204 wherein the synthetic polymer comprises thiol-reactive groups.

207. The method of claim 204 wherein the synthetic polymer comprises *N*-oxysuccinimidyl groups.

208. The method of claim 204 wherein the synthetic polymer is contacted with the tissue prior to raising the pH of the homogeneous solution to a pH of more than about 7.8.

209. The method of claim 204 wherein the synthetic polymer is contacted with the tissue after raising the pH of the homogeneous solution to a pH of more than about 7.8.

210. The method of claim 204 wherein the synthetic polymer is combined with a drug.

211. The method of claim 210 wherein the drug is hydrophobic.

212. The method of claim 211 wherein the drug is in association with a secondary carrier, and the secondary carrier is dispersed in aqueous media.

213. A composition comprising:

a) a synthetic polymer comprising multiple activated groups;
and

b) an aqueous buffer;

wherein the composition is a homogeneous solution having a pH of less than 6.

214. A composition comprising:

a) a synthetic polymer comprising multiple activated groups;
and

b) an aqueous buffer;

wherein the composition is a homogeneous solution having a pH of greater than about 7.8.

215. The compositions of claims 213 or 214 wherein the composition does not contain any polymer that is reactive with the synthetic polymer.

216. The compositions of claims 213 or 214 wherein the composition further comprises a drug.

217. The compositions of claims 213 or 214 wherein the composition further comprises a hydrophobic drug.

218. The compositions of claims 213 or 214 wherein the composition further comprises a hydrophobic drug is association with a secondary carrier.

219. The compositions of claims 213 or 214 wherein the secondary carrier is in the form of a micelle or nanosphere.

220. The compositions of claims 213 or 214 wherein the synthetic polymer comprises alkylene oxide residues.

221. The compositions of claims 213 or 214 wherein the synthetic polymer comprises thiol-reactive groups.

222. The compositions of claims 213 or 214 wherein the synthetic polymer comprises *N*-oxysuccinimidyl groups.

223. The compositions of claims 213 or 214 wherein the synthetic polymer is a 4-arm PEG.

224. The compositions of claims 213 or 214 in sterile form.

225. A method of coating a device comprising:

(a) applying a multifunctional hydroxysuccinimidyl PEG derivative to the surface of the device; and

(b) allowing the derivative to react with functional groups on the device surface.

226. The method of claim 225 wherein the functional surface groups on the device are incorporated into the device using a surface treatment process.

227. The method of claim 226 wherein the surface treatment process is a plasma treatment process.

228. The method of claim 226 wherein the surface treatment process comprises coating the surface of the device with a polymer, wherein the polymer comprises functional groups that can react with the multifunctional hydroxysuccinimidyl PEG derivative.

229. The method of claim 228 wherein the polymer comprises amino groups.

230. The method of claim 229 wherein the polymer is chitosan.

231. The method of claim 229 wherein the polymer is polyethyleneimine.

232. The method of claim 225 wherein the multifunctional hydroxysuccinimidyl PEG derivative is tetra functional poly(ethylene glycol) succinimidyl glutarate.

233. A method of reducing surgical adhesions comprising applying a multifunctional hydroxysuccinimidyl PEG derivative to a tissue surface.

234. The method of claim 233 wherein the multifunctional hydroxysuccinimidyl PEG derivative is in the form of a solution, wherein the solution has a basic pH

235. The method of claim 234 wherein the pH is greater than 8.

236. The method of claim 235 wherein the multifunctional hydroxysuccinimidyl PEG derivative is tetra functional poly(ethylene glycol) succinimidyl glutarate.

237. The method of claim 233 wherein the multifunctional hydroxysuccinimidyl PEG derivative is not in admixture with any other tissue reactive compound.

238. The method of claim 233 wherein the multifunctional hydroxysuccinimidyl PEG derivative is not in admixture with any component that will react with the derivative.

239. A method of reducing surgical adhesions comprising applying a tissue reactive composition consisting essentially of a multifunctional hydroxysuccinimidyl PEG derivative to a tissue surface.

240. A method of reducing surgical adhesions comprising applying a tissue reactive composition consisting of a multifunctional hydroxysuccinimidyl PEG derivative to a tissue surface.